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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ULRICH ZANGER and THOMAS LANG[1]

Appeal 2015-006154
Application 12/404,772
Technology Center 1600

Before ERIC B. GRIMES, JEFFREY N. FREDMAN, and
ULRIKE W. JENKS, *Administrative Patent Judges.*

JENKS, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims directed to assessing a subject's risk of having reduced CYP2B6 protein levels. The Examiner rejects the claims as indefinite and as being directed to patent ineligible subject matter. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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[1] According to Appellants, the real party in interest is Transgenomic, Inc. (App. Br. 2.)

STATEMENT OF THE CASE

Claims 48–61 and 66–68 are on appeal, and can be found in the Claims Appendix of the Appeal Brief.

Claim 48 is representative of the claims on appeal, and reads as follows:

> 48. A method for identifying a subject at risk for reduced CYP2B6 protein levels, the method comprising the steps of:
>
> (a) analyzing a blood sample from a subject for the CYP2B6 allele present at the position corresponding to position 21 of SEQ ID NO: 59;
>
> (b) detecting in a CYP2B6 polynucleotide in the blood sample from the subject the presence of a T at the position corresponding to position 21 of SEQ ID NO: 59; and
>
> (c) identifying the subject having a T at said position as having a risk of reduced CYP2B6 protein levels compared to a subject with a C at said position.

Appellants seek review of the following rejections:

I. claims 50, 54, and 61 under 35 U.S.C. § 112, second paragraph, as being indefinite; and

II. claims 48–61 and 66–68 under 35 U.S.C. § 101 as being directed to patent ineligible subject matter.

ANALYSIS

I. Indefiniteness

Claims 50 and 54

The Examiner's position is that claims 50 and 54 are indefinite because it is "unclear whether the claims further limit the nature of the polynucleotide being detected and require some use of hybridization in its

detection, or whether the claims are intended to require, e.g., the use of a particular type of probe in a hybridization step." Final Act. 3.

Appellants contend that "[i]t is well known in the art of detection of a single nucleotide polymorphism that numerous methods may be employed to detect a particular polymorphism including methods that do not include hybridization of a probe." Appeal Br. 8.

We find Appellants have the better position. We agree with Appellants that there are multiple methods that can detect gene variations. In addition to the restriction endonuclease method suggest by Appellants (*see* Appeal Br. 8), technology also exists that allows for directly sequencing DNA. For example, DNA nanopore sequencing technology available from Oxford Nanopore[2] systems allows for the direct sequencing of DNA and RNA by measuring changes in the current as different nucleotides pass through the nanopore. Therefore, claims 50 and 54 reciting specific probes for hybridizing further limit independent claims 48 and 52 because they narrow the subject matter of the independent claims to a particular detection method. Accordingly, we reverse the rejection of claims 50 and 54.

Claim 61

The Examiner's position is that claim 61 is indefinite because "[t]he specification does not make clear what types of therapies would be considered 'conventional.'" Ans. 5.

Appellants contend that "[t]he specification discloses that CYP2B6 substrates include, among others, antineoplastics, antiestrogens and platelet

[2]Oxford Nanopore Technologies, https://nanoporetech.com/ (last visited January 18, 2016).

aggregation inhibitors." Appeal Br. 8. Appellants contend that equipped with this knowledge the ordinary artisan would understand

> that a subject with reduced substrate metabolizing activity (associated with a particular allelic variant, e.g., T) would be administered a different dose than a subject with a higher metabolizing activity (associated with a different allele, e.g., C), and that heterozygotes may have an intermediate substrate metabolizing activity relative to homozygotes (C/C or T/T).

Id. at 9.

We are not persuaded. Even with the understanding that subjects with allelic variants process their substrates at different rates, this does not clarify the Examiner's question which is directed at what is encompassed by "conventional therapies." Because conventional therapies associated with CYP2B6 are neither disclosed in the Specification nor readily understood from the art generally, we agree with the Examiner's position that the metes and bounds of "conventional" with respect therapies as claimed is not clear. Accordingly, we affirm the Examiner's rejection of claim 61.

II. Patent Ineligible Subject Matter

The Examiner has rejected all of the claims on appeal as directed to patent-ineligible subject matter. The Examiner finds that the claims are directed to "a naturally occurring correlation between a genetic alteration that occurs in nature and risk of reduced protein levels and associated reduced metabolism, i.e., natural principles." Final Act. 5. The Examiner analyzes the claims based on the USPTO's guidance on subject matter eligibility (*id.* at 4–9) and concludes that "the claims as written continue to embrace the practice of well-known, conventional and routine activities on standard biological samples" and thereby do not recite something

significantly different than a judicial exception to patent eligibility. (*Id.* at 8.)

Appellants do not contest that "the occurrence of genetic variation, e.g., in a CYP2B6 gene, is a naturally occurring phenomenon." Reply Br. 3; App. Br. 10. Appellants contend that "the claims ***do not*** 'monopolize' that naturally occurring phenomenon but are in fact directed to a practical application of that phenomenon." Reply Br. 3. Appellants contend that the claims "recite[] a step/element that does not substantially foreclose others from using the judicial exception." Appeal Br. 11. Appellants also argue that the claims "include a specific limitation *other than what is well-understood, routine and conventional*." Reply Br. 4. "[T]he *genetic information* is transformed to allow for stratification of subjects. That stratification can provide for improved treatment of subjects with CYP2D6 [sic] substrates, e.g., by increased efficacy and/or reduced toxicity." *Id.*

We are not persuaded by Appellants' contentions, and agree with the Examiner that claim 48 is directed to a patent-ineligible method as set out in the Final Action mailed October 9, 2013 and Answer which we adopt and incorporate herein by reference. We provide the following additional comment to argument set forth in the Appeal Brief. In *Mayo Collaborative Services v. Prometheus Labs., Inc.*, 132 S.Ct 1289 (2012), the Court considered a claimed method that required administering a drug to a subject, determining the level of a metabolite of the drug in the subject, and using certain thresholds of metabolite level to indicate a need to increase or decrease dosage of the drug. *Id.* at 1295.

The Court noted that the claims "set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and

the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm." *Id.* at 1296. The Court held that the dispositive question was: "do the patent claims add *enough* to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws?" *Id.* at 1297.

The Court held that the claim's "administering" step, "determining" step, and "wherein" clauses did not transform the claim into a patentable application of a natural law, *id.* at 1297–98: "The upshot is that the three steps simply tell doctors to gather data from which they may draw an inference in light of the correlations." *Id.* at 1298.

The Court's analysis in *Mayo* is directly applicable to claim 48, which only requires detecting in the blood sample from the subject the presence of a nucleotide T at the position corresponding to position 21 of the nucleic acid SEQ ID NO: 59 encoding the CYP2B6 polypeptide. Just as in *Mayo*, claim 48 informs a relevant audience of a law of nature and "any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community." *Id.* Thus, claim 48 is directed to a patent-ineligible natural phenomenon or law of nature.

Appellants argue that the stratification of subjects can provide "improved treatment of subjects with CYP2D6 [sic] substrates, e.g., by increased efficacy and/or reduced toxicity." Reply Br. 4. This argument is unpersuasive because the same was true in *Mayo*: "[T]hose in the field did not know the precise correlations between metabolite levels and likely harm or ineffectiveness. The patent claims . . . embody[] researchers' findings that identified these correlations with some precision." *Mayo*, 132 S.Ct at 1295.

Appellants also argue that

> ***identifying a certain specific genetic variation at a particular position*** in a CYP2B6 gene relative to a different genetic composition at that position (or a CYP2B6 protein with a cysteine rather than an arginine at a specific residue), does more than describe the judicial exception with general instructions to use or apply the exception.

Reply Br. 5.

This argument is also unpersuasive. Claim 48 requires "detecting in a CYP2B6 polynucleotide in the blood sample from the subject the presence of a T at the position corresponding to position 21 of SEQ ID NO: 59." This assay step is narrower than the one recited in the claimed method in *Mayo*, which encompassed "determin[ing] the level of the relevant metabolites in the blood, through whatever process the doctor or the laboratory wishes to use." *Mayo*, 132 S.Ct at 1297. We conclude, however, that this distinction does not make claim 48 patent-eligible. The *Mayo* Court noted that "methods for determining metabolite levels were well known in the art. . . . Thus, this step tells doctors to engage in well-understood, routine, conventional activity previously engaged in by scientists who work in the field." *Id.* at 1297–98.

The Court concluded: "Purely 'conventional or obvious' '[pre]-solution activity' is normally not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law." *Id.* at 1298, alteration in original. The same analysis applies here. Detecting the presence of a polynucleotide substitution at a particular location requires only conventional and routine assays. Appellants' Specification, in fact, acknowledges that "the above described methods comprise PCR, ligase chain reaction, restriction digestion, direct sequencing, nucleic acid

amplification techniques, hybridization techniques or immunoassays (Sambrook et al., loc. cit. CSH cloning, Harlow and Lane loc. cit. CSH antibodies)." Spec. 26–27. Thus, the inclusion of the detecting step in the claimed method does not transform the claim into a patent-eligible application of a law of nature.

Finally, with respect to claim 48, Appellants argue that the claimed method includes "identifying the subject having a T at said position as having a risk of reduced CYP2B6 protein levels compared to a subject with a C at said position" and that the significance of that change was unknown. Reply Br. 4. Furthermore, the "stratification [of subjects] can provide for improved treatment of subjects with CYP2D6 [sic] substrates, e.g., by increased efficacy and/or reduced toxicity." *Id.*

This argument is also unpersuasive because claim 48 does not include an active step of administering CYP2B6 substrates to subjects; it merely states that subjects with a particular mutation level in CYP2B6 nucleic acid are at risk for reduced CYP2B6 protein levels. Even if we were to interpret the claim as including making changes to the administration protocol for particular substrates to a subject this would not elevate the claim to encompass patent eligible subject matter. Just as in *Mayo*, claim 48 informs "the relevant audience, namely doctors who treat patients with certain diseases" and "tell[s] the relevant audience about the laws while trusting them to use those laws appropriately where they are relevant to their decisionmaking." *Mayo*, 132 S.Ct at 1297.

For the reasons discussed above, we affirm the rejection of claim 48 under 35 U.S.C. § 101. Claims 49–61 and 66–68 fall with claim 48. 37 C.F.R. § 41.37(c)(1)(iv).

SUMMARY

We reverse the rejection of claims 50 and 54 under 35 U.S.C. § 112, second paragraph, as being indefinite.

We affirm the rejection of claim 61 under 35 U.S.C. § 112, second paragraph, as being indefinite.

We affirm the rejection of claims 48–61 and 66–68 under 35 U.S.C. § 101 as being directed to patent ineligible subject matter.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED